

# Comparison of Anti-Bacterial Efficacy of Silver Diamine Fluoride and sodium fluoride in pre-School Children- An Invivo Study

Divya Shetty, Madhusudan Kaikure, Sowmya B  
Department of Paediatric and Preventive dentistry  
Mangalore, India.

Krithika Shetty, Nayanika Naik, Anusree  
Department of Paediatric and preventive dentistry  
Mangalore, India

**Abstract:-** Dental caries is a multifactorial disease which affects all age bar in different segments of society. With the burden of high-risk caries different approach have been advocated to manage the untreated lesions with affordable cost and noninvasive procedures. The aim of the study is to compare the antibacterial effect of silver diamine fluoride and sodium fluoride varnish. The colony forming units at baseline and after 3 days shows reduction in both the groups. Therefore, significant reduction was seen more in SDF compared to NaF group. After 6 months of reapplication of SDF and NaF varnish, the mean reduction seen in the *S.mutans* count was significant in both the groups. At the end of 6 months, when the intergroup significance was considered, significant reduction was observed in the group of subjects who received SDF application when compared to the group of subjects who received fluoride varnish. It was concluded that there is a reduction in the *S. mutans* count in both the groups after SDF and NaF application. SDF was shown to produce significant reduction. Due to the greater antibacterial efficacy of SDF, it can be used as an effective topical fluoride agent for caries prevention.

## I. INTRODUCTION

Prevalence of dental caries continue to affect different segments of age having severe oral implications which arises from dental caries with negative affect on social, economic status and are considered to be a global burden.<sup>1</sup>

Over the last 70 years, fluorides are used as anti-caries agents<sup>2</sup>. The oral products which contain fluoride and the use of water fluoridation have made decrease in severity of caries. With this as preventive approach there are still disparity seen in all segments of society.<sup>1</sup>

Even though dental services are available, the difficulty to treat young children with traditional treatment approaches and with those requiring special health care needs are affected.<sup>3</sup>

Based on caries management by risk assessment tool (CAMBRA) there are several treatment options to reduce the progression of carious, which includes chemical therapeutics with behavioral modification aimed at altering biofilm behaviors; arresting further demineralization and enhancing remineralization.<sup>4</sup>

There is a need to change the management of caries prevention, which requires efficient, safe, affordable treatment that are available and can be accessible to the affected population.<sup>5</sup>

In the recent times, Arresting caries treatment (ACT) has been advocated to prevail over the problem to manage dental caries in population limited to having less access to oral treatment due to financial constraints and high amount of restorative treatment.<sup>6</sup>

The US Food and Drug Administration approved SDF and it became commercially available as 38% SDF solution.<sup>7,8,9</sup>

SDF is minimally invasive, easy to apply clear liquid, inexpensive and has a high fluoride concentration (44,800 ppm), which is roughly double the strength of 5% sodium fluoride varnish (22,600 ppm) that is commercially available.<sup>4</sup>

The mechanism of action of SDF is not clearly understood. It is said that the chemical composition of SDF which contains silver salts helps in dental sclerosis and silver nitrate kills bacteria, and fluoride remineralizes it.<sup>10</sup>

In addition to the clinical benefit for patients, application of SDF for children with behavioral issues should reduce the clinicians potential legal risk<sup>11</sup>

It satisfies the US Institute of Medicine's quality which aims at being safe in clinical trials that has been used in greater than 3800 individuals and has reported no adverse effects.<sup>3,12</sup> It arrests approximately 80% of treated lesions.<sup>13</sup> It requires a preparation time of less than a minute which is beneficial to different sectors of health professionals.

The present study has not gained much popularity in India. Only limited number of studies have been documented so far.

Therefore, the aim of our study is to compare and evaluate the anti-bacterial efficacy of silver diamine fluoride and sodium fluoride in children.

## II. MATERIALS AND METHODS

This study was conducted in a primary government aided school including children with age groups between 3-6 years in Mangalore, Karnataka following ethical clearance and permission was granted from school. All the students in each classroom from 3-6 years were screened, during which type of oral hygiene practice were evaluated. Use of mouth mirror and explorer were used. So, at the end of screening, 22 children were selected who fulfilled the inclusion criteria. Written informed consent about the purpose of the study was taken from parents before the start of procedure.

Two groups are:

Group A – Silver diamine fluoride

Group B – IRM+ 5% sodium fluoride varnish Ease of Use

### INCLUSION CRITERIA

1. Children whose parents will give the consent for the examination.
2. Children aged 3-6 years.
3. Children who will be present on the day of examination.
4. Deciduous canine and deciduous first and second molars should be present.
5. No history of allergy against silver particles.

### EXCLUSION CRITERIA

1. Children who refuses to participate in dental treatment.
2. Teeth which are grossly decayed i.e., greater than one third of the crown missing.
3. Tooth with pulpal exposure, premature hypermobility and presence of an abscess or sinus, was excluded.
4. Children suffering from oral ulceration, stomatitis, or ulcerative gingivitis.
5. Medically compromised children.
6. Children whose parents are concern towards staining/discoloration of teeth after application of SDF were excluded.

### METHOD OF COLLECTION OF DATA:

Group A: Application of SDF on all deciduous canines and deciduous first and second molars. (n=11)

Group B: Application of NaF on all deciduous canines, deciduous first and second molars. (n=11)

### Baseline evaluation

The following criteria was used to evaluate the patients for baseline examination:

- Tryptone-yeast-cysteine-sucrose-bacitracin agar was used to inoculate salivary *Streptococcus mutans*.
- Saliva collection was done using a cotton swab.
- 0.1ml of saliva was introduced into a sterile vial which contains phosphate buffer saline and was taken to the microbiology laboratory in an icebox where it was processed within 4 hours.

## PROCEDURE FOR FLUORIDE APPLICATION

### Application of SDF (38%)

SDF application on carious tooth of deciduous canine, first and second deciduous molar.

A drop of solution was taken on a cotton pellet and applied for 3-4minutes on all surfaces of teeth.

- In a similar manner, this procedure was carried out on all quadrants.
- After application, patient was instructed to gargle his mouth using normal saline.

### Application of NaF varnish (5%):

1. All carious teeth were restored with IRM. Thorough prophylaxis was done and dried the teeth.
2. The upper and lower quadrants were dried thoroughly and was isolated with cotton rolls.
3. 0.3ml-0.5ml of NaF varnish was applied with cotton applicators and was let to dry for 4 minutes.
4. Patient was instructed to keep the mouth open for 3-4 minutes.
5. To maintain semi solid diet and not to drink or eat for one hour.

The subjects received the second application of NaF after 6 months follow up.

### FOLLOW UP VISITS:

All the subjects in both the groups were followed up and evaluated after 6 months.

Collection of saliva sample was done in both groups after 6 months.

Here, reapplication of SDF and NaF varnish was done.

In both the groups final restoration will be done with glass ionomer.

Saliva sample collection of children was taken in both the groups after 72 hours.

## III. STATISTICAL ANALYSIS

A power analysis was established by G\*power, version 3.0.1 (Franz Faul universitat, Kiel, Germany). A sample size of 22 subjects (11 in each group) would yield 80% power to detect significant differences, with effect size of 0.25 and significance level at 0.05.

- Data was entered in the excel spreadsheet.
- Descriptive statistics like mean, standard deviation and percentages was calculated.
- Inferential statistics like independent sample t test was used to compute between the two groups, repeated measures ANOVA was used to assess change in colony forming units using SPSS version 20 with 80% power.



FIGURE 1:  
38% SILVER DIAMINE FLUORIDE.



FIGURE 2:  
5 % NaF VARNISH



FIGURE 3:  
PHOSPHATE BUFFERED  
SALINE SOLUTION FOR SWAB



FIGURE 4:  
INCLUSION CRITERIA



FIGURE 5:  
SALIVA SAMPLE COLLECTION FROM ONE OF THE SDF  
GROUP

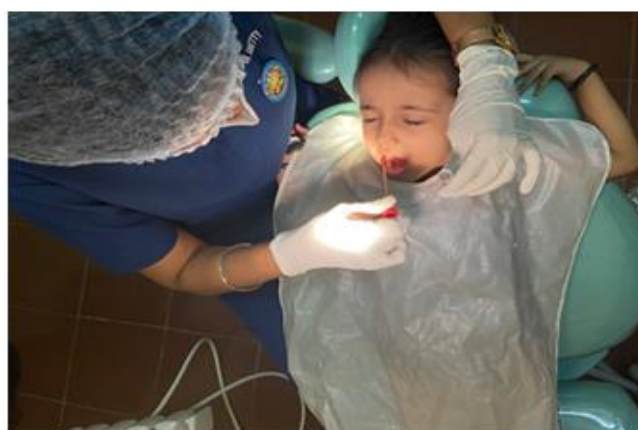


FIGURE 6:  
SALIVA SAMPLE COLLECTION FROM ONE OF THE NaF  
GROUP



FIGURE 7: APPLICATION OF NaF VARNISH



**IV. RESULTS**

**TABLE 1: COMPARISON OF CFU (\*10<sup>6</sup>) BETWEEN THE GROUPS USING INDEPENDENT SAMPLE T TEST AT INITIAL STAGE**

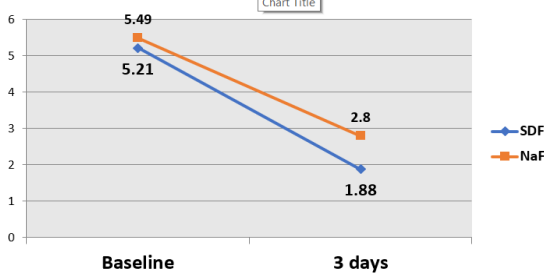
Time intervals	Groups	N	Minimum	Maximum	Mean	Std. Deviation	Mean diff	P value
Baseline	SDF	11	4.06	6.72	5.21	.88	-0.28	0.40
	NaF	11	4.32	6.23	5.49	.63		
3 days	SDF	11	1.22	3.10	1.88	.58	-0.92	0.004*
	NaF	11	1.40	3.78	2.80	.74		

\*significant

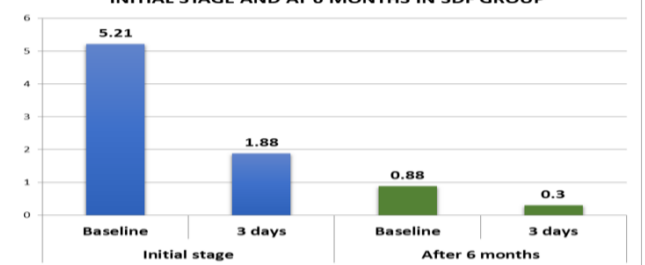
**TABLE 3: TABLE COMPARISON OF CFU (\*10<sup>6</sup>) WITHIN THE GROUP USING PAIRED SAMPLE T TEST AT INITIAL STAGE AND AT 6 MONTHS IN SDF GROUP**

Groups	N	Minimum	Maximum	Mean	Std. Deviation	Mean diff	p value	
Initial stage	Baseline	11	4.06	6.72	5.21	.88	3.32	0.00*
	3 days	11	1.22	3.10	1.88	.58		
After 6 months	Baseline	11	.07	1.70	.88	.53	0.58	0.002*
	3 days	11	.01	.68	.30	.23		

**COMPARISON OF CFU (\*10<sup>6</sup>) BETWEEN THE GROUPS AT INITIAL STAGE**



**COMPARISON OF CFU (\*10<sup>6</sup>) WITHIN THE GROUP AT INITIAL STAGE AND AT 6 MONTHS IN SDF GROUP**



**TABLE 2: COMPARISON OF CFU (\*10<sup>6</sup>) BETWEEN THE GROUPS USING INDEPENDENT SAMPLE T TEST AFTER 6 MONTHS**

**TABLE 2: COMPARISON OF CFU (\*10<sup>6</sup>) BETWEEN THE GROUPS USING INDEPENDENT SAMPLE T TEST AFTER 6 MONTHS**

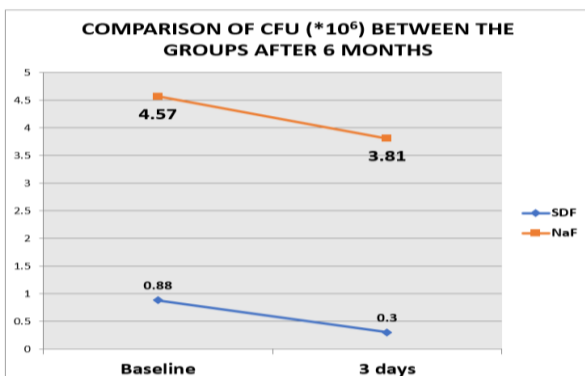
Time intervals	Groups	N	Minimum	Maximum	Mean	Std. Deviation	Mean diff	P value
Baseline(6 months)	SDF	11	.07	1.70	.88	.53	-3.68	0.00*
	NaF	11	3.29	5.86	4.57	.74		
3 days(6 months)	SDF	11	.01	.68	.30	.23	-3.51	0.00*
	NaF	11	2.90	4.90	3.81	.62		

**TABLE 4: COMPARISON OF CFU (\*10<sup>6</sup>) WITHIN THE GROUP USING PAIRED SAMPLE T TEST AT INITIAL STAGE AND AT 6 MONTHS IN NaF GROUP**

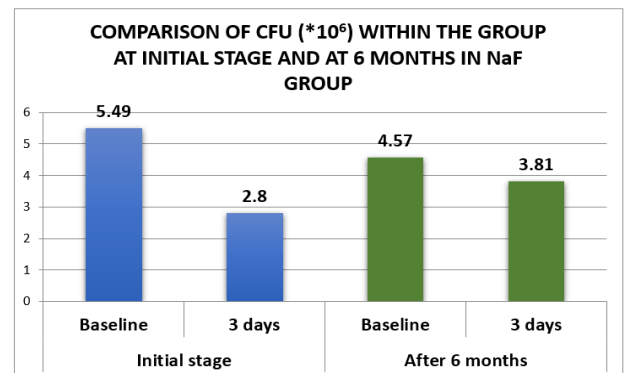
Groups	N	Minimum	Maximum	Mean	Std. Deviation	Mean diff	p value	
Initial stage	Baseline	11	4.32	6.23	5.49	.63	2.68	0.00*
	3 days	11	1.40	3.78	2.80	.74		
After 6 months	Baseline	11	3.29	5.86	4.57	.74	0.77	0.00*
	3 days	11	2.90	4.90	3.81	.62		

\*significant

**COMPARISON OF CFU (\*10<sup>6</sup>) BETWEEN THE GROUPS AFTER 6 MONTHS**



**COMPARISON OF CFU (\*10<sup>6</sup>) WITHIN THE GROUP AT INITIAL STAGE AND AT 6 MONTHS IN NaF GROUP**



## V. DISCUSSION

Management of dental caries requires preventive as well as non-preventive approaches. Non-preventive treatment includes to decelerate the disease process by restoration and mechanical caries removal. Preventive caries involves preventing the caries onset and protecting the teeth from conditions that favour the detrimental impacts on the oral biofilm which includes oral hygiene instructions, nutritional counselling, and fluoride application.<sup>40</sup> Thus, it is essential to manage the early caries progression which can lead to severe pain, traumatic dental procedures for younger age group of children which could be challenging to the Pedodontists and general dental practitioners considering the magnitude of the disease.

Fluoride varnishes are used for preschools as a timely means, as they the ease of application is rapid and well tolerated.<sup>41,42</sup> The motivation to perform present study is related to the fact that dental caries is still prevailing and other preventive approaches might aid the disease prevention, especially when considering the underprivileged population and age group of 3-6 years where minimal intervention is safe and affordable. This study is a randomized controlled trial comparing the antibacterial efficacy of SDF against fluoride varnish NaF.

Several published randomized clinical trials were performed in children 3 years old or older even if it has been documented that SDF reduces caries progression significantly when compared with other modalities. This addresses the research gap and supports the evidence regarding SDF usage in young children with high caries risk.<sup>15</sup> Hence, the age group chosen for this study was 3-6 years, when deciduous canine, first and second deciduous molar is present along with the first window of infectivity.

In 2006, the American dental association mentioned that application of fluoride varnish every 6 months is effective in caries prevention in both deciduous and permanent dentition of children and adolescents.<sup>43</sup> In a study conducted by Chu et al<sup>7</sup> varnish was applied annually, while Llodra et al<sup>37</sup> applied it every 6 months. Hence in this study half yearly application of SDF and NaF varnish was done to compare the antibacterial effect of SDF and NaF on streptococcus mutans count. Streptococcus mutans was the chosen bacterium as it has been advocated in several studies as an indicator for dental caries risk/ caries activity.<sup>44,45,46,47</sup>

As it is known that SDF is effective in preventing and arresting caries, a concentration of 38% was decided. Laboratory studies have mentioned that topical application of a 38% SDF solution can inhibit the growth of cariogenic bacteria. Bijella et al<sup>50</sup> in a study concluded that the frequency of 12% SDF applications on all tooth surface showed influence on the SDF preventive effect irrespective of their caries status. The result showed that the caries incidence after quarterly SDF applications was significantly lower than yearly applications but not significantly different from caries incidence after biannual application. Studies have demonstrated that following SDF applications, an insoluble

protective layer of silver chloride and silver phosphate is formed on the tooth surfaces. This decreases the calcium and phosphorous content from demineralized enamel and dentin. SDF has property such as hardening of dental structures<sup>10,53</sup> by forming fluorohydroxyapatite<sup>54</sup>, by hindering biofilm adherence.<sup>55</sup>

A recent study suggested that SDF application is simpler and cost effective when compared to sealants (Niederman et al 2017). The greater delivery of reagent to a larger population of children with untreated caries is a result of ease of application.<sup>56</sup>

SDF also has a few limitations. It stains the tooth black. Black stain is due to arrest of caries which takes place after SDF application. (Mei et al 2014).<sup>26</sup> The staining property is due to a silver iodine, a white substance sensitive to light. A strategy of avoiding tooth staining is based on applying a solution of KI after SDF, with no influences on SDF efficiency, has been reported.<sup>55</sup> Others currently unreported that the adverse effects include mucosal or gingival inflammation signs, acute or chronic toxicity symptoms, allergic episodes (horst et al, 2016) and discomfort like metallic taste or burning sensation associated with SDF treatment. (Mei et al 2016)<sup>54</sup>. In this experimental study, no such adverse effects are observed. SDF is contraindicated in children who are allergic to silver compounds.

The preventive fraction of NaF was due to frequency of application, duration, and sample size.<sup>25</sup> Hence we selected 5%NaF varnish for this study group. Patil stated that fluoride varnish releases a significant amount of fluoride thereby enhancing the remineralization process and reducing caries.<sup>58</sup>

According to Badjatia et al, the first month of treatment of fluoride varnish is significantly effective in reducing the quantity of bacteria in saliva. These effects can be constant following 3 to 5 months of treatment, but the effects begin to decline after 6 months.<sup>59</sup> Hashemi concluded that applying fluoride varnish once a week for 3 months reduces incidence of caries in the oral cavity.<sup>60</sup> The most effective treatment for increasing saliva pH to reduce caries activity can be achieved by using this varnish for one month.<sup>61</sup> The baseline evaluation of saliva sample was taken before the start of procedure. The procedure of collecting the salivary sample was in accordance to Wan et al.<sup>48</sup> The TYCB agar is the selective media for *S. mutans*, and is the least supportive of non- *S. mutans*.<sup>48,49</sup>

### S. mutans count:

In results, the CFU (colony forming units) at baseline and after 3 days (72 hours) shows reduction in both the groups. Therefore, significant reduction is seen more in SDF group compared to NaF varnish.

When intergroup significance was considered, significant reduction was seen in subjects with SDF application when compared to those who received Sodium fluoride varnish. The results of the present study could strengthen the evidence regarding the use of SDF in young children with high caries risk.

Results obtained is supported by study done by Shalin et al.<sup>2</sup> in which in vivo application of SDF on enamel significantly decreases *S. mutans* counts as compared to sodium fluoride varnish and APF gel.

In this study, the comparison of CFU between the groups using independent sample T test after 6 months was statistically significant with p value < 0.05, and the mean value of streptococcus mutans at baseline for 6 months and 3 days shows reduction in colony forming units.

Jeevarathan et al.,<sup>36</sup> chose to evaluate the *S. mutans* count after 24 hours. It was difficult to judge the effect of fluoride on *S. mutans* count within 24 hours as professional tooth cleaning was done before the application of fluoride. Therefore, in this study *S. mutans* count was evaluated 3 days after application and follow up was done after 6 months.

### Actions of SDF on cariogenic bacteria

Dentine surfaces treated with SDF had significantly less growth of *Streptococcus mutans* than those without SDF treatment. Colony-forming unit counts of monospecies strains of *S. mutans* and *Actinomyces naeslundii* were reduced after application of SDF, with very few bacteria found to be alive. A further study used multispecies cariogenic biofilms consisting of *S. mutans*, *Streptococcus sobrinus*, *L. acidophilus*, *Lactobacillus rhamnosus* and *A. naeslundii*, with the results showing that CFU counts were reduced with SDF treatment.<sup>52</sup> The growth of *S. mutans*, *Streptococcus oralis* and *Lactobacillus casei* was reduced after treatment with SDF.<sup>55</sup> The minimum inhibitory concentration and minimum bactericidal concentration of SDF for *S. mutans* were 33.3 lg/ml and 50.0 lg/ml, respectively<sup>29</sup>, showing that SDF was more effective than silver ammonium nitrate and sodium fluoride.<sup>57</sup>

The results of the present study support the findings of previous invitro studies in which the *S. mutans* counts significantly decreased after SDF application.

Further studies are needed to identify the anti-cariogenic effect of SDF on larger samples.

## VI. CONCLUSION

The following conclusions were drawn:

1. Decrease in streptococcus mutans count was seen in both the group after SDF and NaF application.
2. SDF has the ability to reduce the salivary *S. mutans* when compared to fluoride varnish.
3. Due to the substantial antibacterial efficacy of SDF, it can be used as a topical fluoride agent in caries preventive treatment.

## REFERENCES

[1]. Crystal YO, Niederman R. Evidence-based dentistry update on silver diamine fluoride. *Dental Clinics*. 2019 Jan 1;63(1):45-68.  
 [2]. Shah S, Bhaskar V, Venkataraghavan K, Choudhary P, Ganesh M, Trivedi K. Efficacy of silver diamine fluoride

as an antibacterial as well as antiplaque agent compared to fluoride varnish and acidulated phosphate fluoride gel: An in vivo study. *Indian J Dent Res*. 2013 Sep 1;24(5):575.

- [3]. Crystal YO, Niederman R. Silver diamine fluoride treatment considerations in children's caries management. *Pediatric dentistry*. 2016 Nov 15;38(7):466-71.  
 [4]. Judy Bendit RD, Young DA. Silver diamine fluoride: The newest tool in your caries management toolkit. 2017  
 [5]. Niederman R, ERGUSON M, RDANETA R, ADOVINAC R, Christie D, Tantraphol M, Rasool F. Evidence-based esthetic dentistry. *Journal of Esthetic and Restorative Dentistry*. 1998 Sep;10(5):229-34.  
 [6]. Yee R, Holmgren C, Mulder J, Lama D, Walker D, van Palenstein Helderman W. Efficacy of silver diamine fluoride for arresting caries treatment. *J dent res*. 2009;88(7):644-7  
 [7]. Chu CH, Lo EC, Lin HC. Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin caries in Chinese pre-school children. *Journal of dental research*. 2002 Nov;81(11):767-70.  
 [8]. ElevateOralCare. Advantage arrest SDF 38% bottle. Available at:<http://www.elevateoralcare.com/dentist/AdvantageArrest/Advantage-Arrest-Silver-Diamine-Fluoride-38>. Accessed November 1, 2018.  
 [9]. ElevateOralCare. Advantage arrest: SDF 38% product package insert. Available at: [http://www.elevateoralcare.com/site/images/AA\\_PI\\_040715.pdf](http://www.elevateoralcare.com/site/images/AA_PI_040715.pdf). Accessed November 1, 2018.  
 [10]. Rosenblatt A, Stamford TCM, & Niederman R (2009) Silver diamine fluoride: A caries "silver-fluoride bullet." *Journal of Dental Research* 88(2) 116-125.  
 [11]. Niederman R, Richards D, Brands W. The changing standard of care. *J Am Dent Assoc*. 2012;143(5):434-7.  
 [12]. D. Duangthip, M.H.T. Fung, M.C.M. Wong, et al. Adverse effects of silver diamine fluoride treatment among preschool children *J Dent Res*, 97 (4) (2018), pp. 395-401.  
 [13]. Gao SS, Zhao IS, Hiraishi N, Duangthip D, Mei ML, Lo EC, Chu CH. Clinical trials of silver diamine fluoride in arresting caries among children: a systematic review. *JDR Clinical & Translational Research*. 2016 Oct;1(3):201-10.  
 [14]. Sorkhndini P, Gregory RL, Crystal YO, Tang Q, Lippert F. Effectiveness of in vitro primary coronal caries prevention with silver diamine fluoride-Chemical vs biofilm models. *Journal of Dentistry*. 2020 Aug 1;99:103418.  
 [15]. Mabangkhu S, Duangthip D, Hung CC, Phonghanyudh A, Jirattanasopha V. A randomized clinical trial to arrest dentin caries in young children using silver diamine fluoride. *Journal of Dentistry*. 2020 May 16:103375.  
 [16]. Uchil SR, Suprabha BS, Suman E, Shenoy R, Natarajan S, Rao A. Effect of three silver diamine fluoride application protocols on the microtensile bond strength of resin-modified glass ionomer cement to carious dentin in primary teeth. *Journal of Indian Society of*

- Pedodontics and Preventive Dentistry. 2020 Apr 1;38(2):138.
- [17]. Lou Y, Darvell BW, Botelho MG. Antibacterial effect of silver Diammine fluoride on cariogenic organisms. The journal of contemporary dental practice. 2018 May 1;19(5):591-8.
- [18]. Vollú AL, Rodrigues GF, Teixeira RV, Cruz LR, dos Santos Massa G, de Lima Moreira JP, Luiz RR, Barja-Fidalgo F, Fonseca-Gonçalves A. Efficacy of 30% silver diamine fluoride compared to atraumatic restorative treatment on dentine caries arrestment in primary molars of preschool children: A 12-months parallel randomized controlled clinical trial. Journal of dentistry. 2019 Sep 1;88:103165.
- [19]. Tirupathi S, Nirmala SV, Rajasekhar S, Nuvvula S. Comparative cariostatic efficacy of a novel Nano-silver fluoride varnish with 38% silver diamine fluoride varnish a double-blind randomized clinical trial. Journal of Clinical and Experimental Dentistry. 2019 Feb;11(2):e105.
- [20]. Mohammadi N, Far MH. Effect of fluoridated varnish and silver diamine fluoride on enamel demineralization resistance in primary dentition. Journal of Indian Society of Pedodontics and Preventive Dentistry. 2018 Jul 1;36(3):257.
- [21]. Bimstein E, Damm D. Human primary tooth histology six months after treatment with silver diamine fluoride. Journal of Clinical Pediatric Dentistry. 2018;42(6):442-4.
- [22]. Vinson LA, Gilbert PR, Sanders BJ, Moser E, Gregory RL. Silver Diamine Fluoride and Potassium Iodide Disruption of In Vitro Streptococcus mutans Biofilm. Journal of Dentistry for Children. 2018 Sep 15;85(3):120-4.
- [23]. Wierichs RJ, Westphal S, Lausch J, Meyer-Lückel H, Esteves-Oliveira M. Influence of highly concentrated fluoride dentifrices on remineralization characteristics of enamel in vitro. Clinical oral investigations. 2018 Jul 1;22(6):2325-34.
- [24]. Pratas PL. Efeito de óleos de origem vegetal na inibição de bactérias cariogénicas: estudo in vitro (Doctoral dissertation).
- [25]. Mishra P, Fareed N, Battur H, Khanagar S, Bhat MA, Palaniswamy J. Role of fluoride varnish in preventing early childhood caries: A systematic review. Dental research journal. 2017 May;14(3):169.
- [26]. Mei ML, Ito L, Cao Y, Lo EC, Li QL, Chu CH. An ex vivo study of arrested primary teeth caries with silver diamine fluoride therapy. Journal of dentistry. 2014 Apr 1;42(4):395-402.
- [27]. François P, Greenwall-Cohen J, Le Goff S, Ruscassier N, Attal JP, Dursun E. Shear bond strength and interfacial analysis of high-viscosity glass ionomer cement bonded to dentin with protocols including silver diamine fluoride. Journal of Oral Science. 2020;62(4):444-82.
- [28]. Baothman A, Assery M. Effect of modified 5% sodium fluoride on the surface roughness and hardness of the enamel of primary incisors: An in vitro study. Saudi Journal of Oral Sciences. 2017 Jan 1;4(1):28.
- [29]. Fung MH, Duangthip D, Wong MC, Lo EC, Chu CH. Arresting dentine caries with different concentration and periodicity of silver diamine fluoride. JDR Clinical & Translational Research. 2016 Jul;1(2):143-52.
- [30]. Rechmann P, Bekmezian S, Rechmann BM, Chaffee BW, Featherstone JD. MI Varnish and MI Paste Plus in a caries prevention and remineralization study: a randomized controlled trial. Clinical Oral Investigations. 2018 Jul 1;22(6):2229-39.
- [31]. Gavrilă L, Maxim A, Balan A, Stoleriu S, Sandu AV, Serban V, Savin C. Comparative study regarding the effect of different remineralizing products on primary and permanent teeth enamel caries lesions. Revista de Chimie. 2015 Aug 1;66(8):1159-
- [32]. Duangthip D, Fung MH, Wong MC, Chu CH, Lo EC. Adverse effects of silver diamine fluoride treatment among preschool children. Journal of dental research. 2018 Apr;97(4):395-401.
- [33]. Mei ML, Ito L, Cao Y, Li QL, Lo EC, Chu CH. Inhibitory effect of silver diamine fluoride on dentine demineralisation and collagen degradation. Journal of dentistry. 2013 Sep 1;41(9):809-17.
- [34]. Zhi QH, Lo EC, Lin HC. Randomized clinical trial on effectiveness of silver diamine fluoride and glass ionomer in arresting dentine caries in preschool children. Journal of dentistry. 2012 Nov 1;40(11):962-7.
- [35]. Yee R, Holmgren C, Mulder J, Lama D, Walker D, van Palenstein Helder W. Efficacy of silver diamine fluoride for arresting caries treatment. Journal of dental research. 2009 Jul;88(7):644-7.
- [36]. Jeeva Rathan J. Effect of Fluoride Varnish on Streptococcus Mutans Count in Plaque of Caries Free Children using Dentocult SM Strip Mutans Test: A Randomized Controlled Triple Blind study (Doctoral dissertation, Meenakshi Ammal Dental College, Chennai).
- [37]. Llodra JC, Rodriguez A, Ferrer B, Menardia V, Ramos T, Morato M. Efficacy of silver diamine fluoride for caries reduction in primary teeth and first permanent molars of schoolchildren: 36-month clinical trial. Journal of dental research. 2005 Aug;84(8):721-4.
- [38]. Chedid SJ, Cury JA. Effect of 0.02% NaF solution on enamel demineralization and fluoride uptake by deciduous teeth in vitro. Brazilian oral research. 2004 Mar;18(1):18-
- [39]. Religa ZC, Wilson S, Ganzberg SI, Casamassimo PS. Association between bispectral analysis and level of conscious sedation of pediatric dental patients. Pediatr Dent. 2002 May 1;24(3):221-6.
- [40]. Council, O. Caries-risk Assessment and Management for Infants, Children, and Adolescents. Pediatr. Dent. 39, 197–204 (2017).
- [41]. Carvalho DM, Salazar M, Oliveira BH, Coutinho ES. Fluoride varnishes and decrease in caries incidence in preschool children: A systematic review. Rev Bras Epidemiol. 2010;13:139–49.
- [42]. Petersson LG, Twetman S, Dahlgren H, Norlund A, Holm AK, Nordenram G, et al. Professional fluoride varnish treatment for caries control: A systematic review of clinical trials. Acta Odontol Scand. 2004;62:170–6.



- [43]. American Dental Association Council on Scientific Affairs. Professionally applied topical fluoride: Evidence-based clinical recommendations. *J Am Dent Assoc* 2006;137:1151-9.
- [44]. Yamaga R, Nishino M, Yoshida S, Yokomizo I. Diammine silver fluoride and its clinical application. *J Osaka Univ Dent Sch* 1972;12:1-20
- [45]. Guo L, Shi W. Salivary biomarkers for caries risk assessment. *Journal of the California Dental Association*. 2013 Feb;41(2):107.
- [46]. Klock B, Krasse B. Effect of caries-preventive measures in children with high numbers of *S. mutans* and lactobacilli. *European Journal of Oral Sciences*. 1978 Aug;86(4):221-30.
- [47]. Law V, Seow WK. A longitudinal study of 0.2% chlorhexidine gel for removal of mutans streptococci infection in preschool children. *Australian dental journal*. 2007 Mar;52(1):26-32.
- [48]. Wan AK, Seow WK, Walsh LJ, Bird PS. Comparison of five selective media for the growth and enumeration of *Streptococcus mutans*. *Aust Dent J* 2002;47:21-6
- [49]. Van Palenstein Helderma WH, Ijsseldijk M, Huis in't Veld JH. A selective medium for the two major subgroups of the bacterium *Streptococcus mutans* isolated from human dental plaque and saliva. *Arch Oral Biol* 1983;28:599-603.
- [50]. Oliveira BH, Rajendra A, Veitz-Keenan A, Niederman R. The effect of silver diamine fluoride in preventing caries in the primary dentition: a systematic review and meta-analysis. *Caries research*. 2019;53(1):24-32.
- [51]. Greenwall-Cohen J, Greenwall L, Barry S. Silver diamine fluoride-an overview of the literature and current clinical techniques. *British Dental Journal*. 2020 Jun;228(11):831-8.
- [52]. Alves S, Maria T, Silva CA et al. Atividade Antimicrobiana de Produtos Fluoretados sobre Bactérias Formadoras do biofilme Dentário: Estudo in vitro. *Pesqui Bras Odontopediatria Clin Integr* 2010 10: 209–216.
- [53]. Targino AG, Flores MA, dos Santos Junior VE, Bezerra FD, de Luna Freire H, Galembeck A, Rosenblatt A. An innovative approach to treating dental decay in children. A new anti-caries agent. *Journal of Materials Science: Materials in Medicine*. 2014 Aug 1;25(8):2041-7.
- [54]. Mei ML, Nudelman F, Marzec B, Walker JM, Lo EC, Walls AW, Chu CH. Formation of fluorohydroxyapatite with silver diamine fluoride. *Journal of dental research*. 2017 Sep;96(10):1122-8.
- [55]. Zhao IS, Gao SS, Hiraishi N, Burrow MF, Duangthip D, Mei ML, Lo EC, Chu CH. Mechanisms of silver diamine fluoride on arresting caries: a literature review. *International dental journal*. 2018 Apr;68(2):67-76.
- [56]. Horst JA, Ellenikotis H, Milgrom PM, UCSF Silver Caries Arrest Committee. UCSF protocol for caries arrest using silver diamine fluoride: rationale, indications, and consent. *Journal of the California Dental Association*. 2016 Jan;44(1):16.
- [57]. Targino AGR, Flores MAP, dos Santos Junior VE et al. An innovative approach to treating dental decay in children. A new anti-caries agent. *J Mater Sci Mater Med* 2014 25: 2041–2047.
- [58]. Alhamed M, Almalki F, Alselami A, Alotaibi T, Elkatehy W. Effect of different remineralizing agents on the initial carious lesions—A comparative study. *The Saudi Dental Journal*. 2020 Dec 1;32(8):390-5
- [59]. Badjatia S, Badjatia RG, Thanveer K, Krishnan AC. Effects of fluoride varnish on *Streptococcus mutans* count in saliva. *International journal of clinical pediatric dentistry*. 2017 Jan;10(1):62.
- [60]. Hashemi Z, Malek Mohammadi T, Poureslami H, Sharifi H. The effect of topical iodine and fluoride varnish combination in preventing early childhood caries: A pilot study. *Journal of Dental Materials and Techniques*. 2015;4(4):167-72.
- [61]. Apriani A, Widyanman AS, Budiyananti EA, Roeslan BO. Caries activity and pH level changes after fluoride varnish and casein phosphopeptides-amorphous calcium phosphate application on children's saliva. *Contemporary Clinical Dentistry*. 2020 Apr;11(2):126.
- [62]. Bibby BG. A new approach to caries prophylaxis. *Tufts Dent Outlook* 1942;15:4-8.